REMARKS

Applicants have amended claims 1, 4, 14, and 16 and added new claims 18-24 to more particularly point out and distinctly claim the subject matter of this invention. Support for the amended claims and the new claims can be found at various places in the specification.[1] Applicants have also amended claims 6, 7, and 9 to rectify minor deficiencies. Claims 2, 3, 10-13, 15, and 17 have been cancelled. In addition, Applicants have amended the specification to correct several typographical errors.

Claims 1, 4-9, 14, 16, and 18-24 are now pending. Reconsideration of the application, as amended, is requested in view of the remarks below.

Rejection under 35 U.S.C. 112, second paragraph

The Examiner rejects claims 1, 3, 4, 7, and 10-17 on one or more grounds. Applicants will traverse each ground below.

Claims 1 and 3 are rejected for being incomplete. According to the Examiner, both claims omit essential steps to accomplish the alleged purpose of "assessing aspirin resistance." Applicants have incorporated the limitations of claims 2 and 3 into claim 1. It is submitted that amended claim 1 includes all essential steps for determining aspirin resistance.

Claims 3 and 7 are rejected because the terms "the second, third or fourth quartile" and "the immunoassay" recited therein lack antecedent basis. Claim 3 has been cancelled. Applicants have amended claim 7 to correct the deficiency pointed out by the Examiner.

Claims 4, 10-13, and 17 are rejected for being unclear about what baseline is used to assess relative risk of a cardiovascular event. Claims 10-13 and 17 have been cancelled. Applicants have amended claim 4 to specify the baseline quartile used in assessing relative risk of a cardiovascular event.

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[1] For example, support for amended claims 1, 4, 14, and 16 appears at page 11, line 13 through page 12, line 13 and Figure 1; support for new claim 18 appears at page 10, lines 17-19; and support for new claims 19-24 appears in Table 3 at page 33.

Referring to claims 10-15, the Examiner points out a number of typographical errors. Claims 10-13 and 15 have been cancelled. Applicants have amended claim 14 to change "dihydro" to "dehydro."

Finally, the Examiner rejects claim 14, asserting that the phrase "providing a readout" recited therein is vague. Applicants have replaced this phrase with "determining" to promote clarity.

Rejection under 35 U.S.C. 112, first paragraph

The Examiner rejects claims 10-13 and 16, asserting that they fail to comply with the enablement requirement. More specifically, he alleges that "[t]he claims contains subject matter that was not described in the specification in such a way as enable one skilled in the art to which it pertains [] to make and/or use the invention." See the Office Action, page 4, lines 11-13.

Claims 10-13 have been cancelled. Applicants have amended claim 16 to correct several errors. Amended claim 16 covers a method for assessing specific levels (1.0, 1.3, 1.4, or 1.8 times) of relative risk of a cardivascular event by comparing the concentration of thromboxane B2 in a sample with four quartiles, each containing a specific range (less than 15.1, 15.1 to 21.8, 21.9 to 33.8, or greater than 33.9 pg/nm of creatinine). The specification provides general guidance on how to determine the concentration of thromboxane B2 in a sample and compare the concnetration with those of the four quartiles, each containing certain range of creatinines. In addition, it teaches that the relative risk of a cardiovascular disease is 1.3 times for a concentration in the second quartile, 1.4 times for a concentration in the third quartile, and 1.8 times for a concentration in the fourth quartile, as compared to that for a concentration in the first quartile. See page 11, lines 24-26. Thus, one skilled in the art would be enabled to practice the method of claim 16. In other words, amended claim 6 meets the enablement requirement.

Rejections under 35 U.S.C. 102(b)

The Examiner rejects claims 1, 4-9, and 17 for anticipation, relying on Ens, WO 01/31052 (Ens). Claim 17 has been cancelled. Claims 1 and 4, the two independent claims, will be discussed first.

Amended claim 1 covers a method for assessing aspirin resistance. The method includes determining the concentration of a metabolite of thromboxane A2 in a sample; comparing this concentration to a predetermined set of concentration quartiles having first, second, third, and fourth quartiles; and determining within which quartile the sample concentration falls. If the sample concentration falls within the second, third, or fourth quartile, it is indicative of aspirin resistance of various degrees.

Amended claim 4 covers a method for assessing relative risk of a cardiovascular event in a patient taking aspirin. The method includes comparing the concentration of the metabolite to a predetermined set of concentration quartiles; and determining whether the concentration falls within the first, second, third, or fourth quartile. The relative risk is increased for a concentration in the second, third, or fourth quartile relative to a concentration in the first quartile.

The methods of claims 1 and 4 both include a step of comparing the concentration of metabolite in a sample with a predetermined set of concentration quartiles.

Ens discloses a method for identifying a minimal aspirin dose by measuring thrommbocxane B_2 metabolite levels in a patient to determine an optimum dose for platelet inhibition. Nowhere in Ens is it taught or suggested using **a predetermined set of concentration quartiles** to determine aspirin resistance or to assess relative risk of a cardiovascular event. Thus, Ens does not anticipate amended claims 1 and 4, both of which rely on **a predetermined set of concentration quartiles** to determine aspirin resistance or assess relative risk of a cardiovascular event.

For the same reasons set forth above, claims 5-9, dependent from claim 4, are also not anticipated by Ens.

Rejection under 35 U.S.C. 103(a)

The Examiner rejects claims 2, 3, and 10-16 for obviousness, relying on Ens, Cipollone et al. 102 Circulation (2000) 1007 (Cipollone), and Armitage et al., Encyclopedia of Biostatics (1998) (Armitage). Claims 2, 3, 10-13, and 15 have cancelled. Only claims 14 and 16 will be discussed.

Claim 14, as amended, covers a method for assessing relative risk of a cardiovascular event in a patient taking aspirin by comparing the concentration of the metabolite of thromboxane A2 to a predetermined set of concentration quartiles; and determining whether the concentration falls within the first, second, third, or fourth quartile. The first quartile contains a concentration of thromboxane B2 at less than 15.1 ng/mmol creatinine, the second quartile contains a concentration of thromboxane B2 at 15.1 to 21.8 ng/mmol creatinine, the third quartile contains a concentration of thromboxane B2 at 21.9 to 33.7 ng/mmol creatinine, and the fourth quartile contains a concentration at equal to or greater than 33.8 ng/mmol creatinine.

As pointed out above, Ens discloses a method for identifying a minimal aspirin dose by measuring thrommbocxane B_2 metabolite levels in a patient to determine an optimum dose for platelet inhibition, and does not suggest using a predetermined set of concentration quartiles, let alone specific concentration ranges of thromboxane B2 relative to creatinine recited in claim 14.

Cipollone teaches a normal range of 17.0-28.3 ng/mmol of 11-dehydro-thromboxane B2 in patients taking aspirin. Like Ens, it also does not suggest using a set of four concentration quartiles. While Armitage teaches using quartiles as a useful tool for modeling risk relationship, it is silent on the specific concentration range of 11-dehydro-thromboxane B2 relative to creatinine in each quartile recited in claim 14. As none of Ens, Cipollone, and Armitage suggests the concentration range of 11-dehydro-thromboxane B2 relative to creatinine in each quartile as recited in claim 14, a combination of these references fails to do so. Claim 14 is clearly not rendered obvious by these references.

Claim 16 depends from claim 14. For the same reasons set forth above, it is also not obvious over the cited references.

CONCLUSION

For the reasons set forth above, Applicants submit that the grounds for the objections and rejections asserted by the Examiner have been overcome and claims 1, 4-9, 14, 16, and 18-24, as pending, cover subject matter that is novel and unobvious over the prior art. Applicants request that all pending claims be allowed.

Enclosed is a $55 check for the Petition for Extension of Time fee. Please apply any other charges or credits to deposit account 06-1050.

Respectfully submitted,

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